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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,647	07/30/2003	Junya Yoneda	239534US0CONT	6857

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EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	02/27/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/27/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/629,647	YONEDA ET AL.	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-20 and 22-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-20 and 22-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed November 27, 2006 presents remarks and arguments submitted to the office action mailed July 27, 2006 is acknowledged.

Applicant's amendments submitted November 27, 2006 is acknowledged wherein claims 1-13 are withdrawn, 14-20 are amended, 21 is canceled, and 22-29 are added.

Applicant's arguments over the 35 U.S.C. 112 rejections of claims 14-21 is persuasive due to amendments made to claims. Therefore, the rejection is herewith withdrawn.

Applicant's arguments over the 35 U.S.C. 102 (b) rejection of claims 14-16, 20-21 over Moretti (WO 97/05862) is persuasive due to amendments made to claims. Therefore, the rejection is herewith withdrawn.

Applicant's arguments over the 35 U.S.C. 102 (b) rejection of claims 14-17, and 20 over Meisner (US Pat No. 4,772,591) is persuasive due to amendments made to claims. Therefore, the rejection is herewith withdrawn.

Applicant's arguments over the 35 U.S.C. 102 (b) rejection of claim 14 over Akimoto et al. (Pat No. 5,834,512) is persuasive due to amendments made to claims. Therefore, the rejection is herewith withdrawn.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 18 and 19 over Moretti (WO 97/05862) and further in view of Fischer et al. (US Pat. No. 3,950,529) and Ansel et al. is persuasive due to amendments made to claims. Therefore, the rejection is herewith withdrawn.

The following new rejections are made:

Claim Rejections - 35 USC § 11 2

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any : person skilled in the ad to which it pertains, or with which It is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-29 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not provide sufficient information that inflammatory diseases are preventable using the method of administering an effective amount of ornithine and one or more branched amino acids to a subject in need thereof.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention, (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims', (6) the amount of direction or guidance presented', (7) the presence or absence of working examples', and (8) the quantity of experimentation necessary. When the

above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1). The Nature of the Invention: the rejected claims 22-29 are drawn to, "a method for preventing an inflammatory disease which comprises administering an effective amount of ornithine and one or more branched amino acids to a subject in need thereof. "

(2). The state of the prior art: In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of **preventing** an inflammatory disease. The state of the art for the treatment of inflammatory diseases is relatively high.

(3). The predictability or unpredictability of the art: the art does not enable a person of ordinary skill in the art to make and use the claimed invention without resorting to undue experimentation.

The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing an inflammatory disease. The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not as of yet reasonably possible with most diseases/disorders, the specification is viewed as lacking an adequate enablement of where inflammatory diseases may be actually prevented.

(4). The breadth of the claims: the claims encompass a method for preventing an inflammatory disease which comprises administering an effective amount of ornithine and one or more branched amino acids to a subject in need thereof. Applicant fails to set forth the criteria that define prevention of the disease. Thus, the breadth of the claim is over broad.

(5). The amount of direction or guidance presented: does not provide any guidance in terms of preventing an inflammatory disease.

(6). The presence or absence of working examples: applicant does not provide any working examples for the prevention of an inflammatory disease. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the preventative effects of the instant composition.

(7). The quantity of experimentation necessary: the quantity of experimentation would be an undue burden to one of ordinary skill in the art and amount to the trial and error type of experimentation. Thus, factors such as "sufficient working examples, "the level of skill in the art' and "predictability" etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

In view of the breadth of the claims, unpredictability of preventing an inflammatory disease, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of

experimentation to use the instantly claimed invention commensurate in scope with the claims.

The burden of enabling one skilled in the art to prevent an inflammatory disease would be much greater than that enabling the treatment. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing an inflammatory disease. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed compound ornithine and one or more branched amino acids for preventing an inflammatory disease.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-17, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moretti (WO 97/05862) and Meisner (US Pat No. 4,772,591).

Moretti teaches the oral or parenteral administration of the amino acid ornithine in the treatment of inflammatory bowel disease, hepato-splenomegaly associated with inflammatory disease, rheumatoid arthritis, and connective tissue disease (inflammatory diseases) (see claims 1,2,4,12-14, and 15; p. 9-11).

Meisner teaches an amino acid used in a composition to treat tissue degenerative inflammations and inflammatory diseases is valine (branched amino acid)

(column 4, lines 42-60). Exemplary inflammatory diseases include osteoarthritis. The composition is administered topically and orally (column 6, lines 15 and 40). In the oral form, the substance mixture is formulated into pharmaceutically acceptable dosage forms such as powders, tablets, or capsules (see column 6, lines 45-49).

The use of the amino acid ornithine in combination with valine (branched amino acid) would have been prima facie obvious to one of ordinary skill in the art because it was well known in the art that both ornithine and valine are used in treatment of inflammatory diseases, and even more specifically in the treatment of arthritic diseases, as recited in claim 29. Motivation to administer both ornithine and valine in combination flows logically from the efficacy demonstrated in the prior art as hypertension compounds used in the treatment of inflammatory diseases. The skilled artisan would have reasonably concluded, in light of the shared efficacy in treatment of inflammatory diseases, that the concomitant administration of ornithine and valine would have been reasonably expected to achieve, at minimum, additive, if not synergistic, effects when combined. It is further noted that in the absence of evidence to the contrary, it is generally prima facie obvious to use in combination two or more agents that have previously been used separately for the same purpose. See In re Kerkhoven, 205 USPQ 1069 (CCPA).

Claims 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moretti (WO 97/05862) and Meisner (US Pat No. 4,772,591) as applied to claims 14-17, 20 above, and further in view of Fischer et al. (US Pat. No. 3,950,529) and Ansel et al. (Pharmaceutical Dosage Forms and Drug Delivery Systems 7th Edition p 227).

Moretti et al. and Meisner is as discussed above.

Moretti et al. and Meisner fail to teach ornithine and a branched amino acids in a food or a drink.

Fischer teaches an amino acid formulation comprised of isoluecine, leucine, and valine formulated for intravenous or oral administration (see abstract). For oral consumption, the amino acid mixture, are made into edible food preparations in the form of palatable liquid drinks or semisolid foods.

Additionally, Ansel et al. teaches, "solid dosage forms are best taken with a glassful of water or a beverage. Further, the reference teaches an ordinary tablet crushed or a capsule opened helps "facilitate ease of administration, any unpleasant drug taste may be masked by mixing with custards, yogurt, rice pudding, other soft food, or fruit juice (p. 227, column 2, paragraph 5)."

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer ornithine and branched amino acids with a food or drink because Morreti et al. teaches amino acid compositions comprising leucine, isoleucine, and valine incorporated with food preparations. The motivation to administer ornithine and branched amino acids with a food or drink is because Ansel et al. teaches that for ease of administration and avoidance of unpleasant tastes drugs may be administered with various foods and drinks. Therefore, a skilled artisan would have reasonable expectation of success in incorporating ornithine and branched amino acids with a food or drink.

Response to Arguments

Applicant's arguments filed November 27, 2006 have been fully considered.

In regard to the applicant's arguments made against the 35 U.S.C. § 112, first paragraph, Examiner states the enablement for methods of prevention of inflammatory diseases lacks support from the applicant's specification or prior art. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

The burden of enabling the prevention of inflammatory diseases (i.e., the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those humans susceptible to such conditions. In the instant case, the specification does not provide guidance as to how one skilled in the art would go about preventing those patients susceptible to inflammatory diseases within the scope of the presently claimed invention. Nor is there any guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed method in preventing the inflammatory diseases among the patients. The specification fails to enable "prevention", and undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed method for the prevention of inflammatory diseases.

Applicant's argument that the references **generically** disclose the possibility of using either ornithine, valine, or leucine respectively, in the prophylaxis or treatment of many disorders, including inflammatory diseases is not persuasive. It is not the mere possibility that the reference teaches the treatment of inflammatory diseases; the

reference in fact indicates that the prior art treats inflammatory disorders. This would indicate that a skilled artisan would have known that such amino acids would treat inflammatory diseases.

In response to Applicant's arguments that Fischer et al. (US Pat. No. 3,950,529) and Ansel et al. do not compensate for the aforementioned deficiencies in the disclosure of Moretti, Meisner, and Akimoto. Examiner respectfully states that the references are cited merely to show that it is well known in the prior art that active ingredients are added to drinks and food preparations. The motivation to administer ornithine and branched amino acids with a food or drink is because Ansel et al. teaches that for ease of administration and avoidance of unpleasant tastes drugs may be administered with various foods and drinks. Therefore, a skilled artisan would have reasonable expectation of success in incorporating ornithine and branched amino acids with a food or drinks.

The arguments are not persuasive and the rejection is made **FINAL**.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER